UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/820,430	04/08/2004	Charli Kruse	B1180/20026	7174

3000 7590 12/15/2006

CAESAR, RIVISE, BERNSTEIN,
COHEN & POKOTILOW, LTD.
11TH FLOOR, SEVEN PENN CENTER
1635 MARKET STREET
PHILADELPHIA, PA 19103-2212

EXAMINER	
HAMA, JOANNE	
ART UNIT	**PAPER NUMBER**
1632	

DATE MAILED: 12/15/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/820,430	KRUSE, CHARLI	
	Examiner	Art Unit	
	Joanne Hama, Ph.D.	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 September 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☐ Claim(s) *1-47* is/are pending in the application.

4a) Of the above claim(s) *15-47* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-14* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *25 August 2006* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election without traverse of Group 1 in the reply filed on September 25, 2006 is acknowledged. Regarding the species election, Applicant elects acinar tissue from the pancreas, **without** traverse.

Claims 15-47 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected inventions, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on September 25, 2006.

Claims 1-14 are under consideration.

It is noted that the Examiner of record has changed.

Drawings

The drawings filed August 25, 2005 are objected to because Figures 4 and 5 are dark. Corrected drawing sheets in compliance with 37 CFR 1.121(d) are required in reply to the Office action to avoid abandonment of the application. Any amended replacement drawing sheet should include all of the figures appearing on the immediate prior version of the sheet, even if only one figure is being amended. The figure or figure number of an amended drawing should not be labeled as "amended." If a drawing figure is to be canceled, the appropriate figure must be removed from the replacement sheet, and where necessary, the remaining figures must be renumbered and appropriate changes made to the brief description of the several views of the drawings for

consistency. Additional replacement sheets may be necessary to show the renumbering of the remaining figures. Each drawing sheet submitted after the filing date of an application must be labeled in the top margin as either "Replacement Sheet" or "New Sheet" pursuant to 37 CFR 1.121(d). If the changes are not accepted by the examiner, the applicant will be notified and informed of any required corrective action in the next Office action. The objection to the drawings will not be held in abeyance.

Priority

Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file. German Application 103 28 280.7 has been received.

Information Disclosure Statement

Applicant filed an Information Disclosure Statement (IDS) on January 10, 2005. The IDS has been considered.

The publication Kruse et al. 2004 (page 3 of 4 of the IDS) is missing publication information. The Examiner has indicated the missing information on the IDS. Applicant is requested to amend and resubmit a corrected IDS.

Claim Objections

Claims 4, 6 are objected to because of the following informalities: claims 4 and 6 encompass non-elected subject matter, i.e. a variety of glandular tissues from which the

cells are derived (e.g. claim 4) and a variety of sites from which the acinar tissue is derived (e.g. claim 6). Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-14 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for

rat and human isolated pluripotent adult stem cells obtained by mechanically and enzymatically breaking up acinar tissue from pancreas and culturing for several weeks in culture vessels, during which time differentiated cells are removed, wherein said pluripotent adult stem cells differentiate into nerve cells (expressing PGP 9.5 and NF), glial cells (expressing S100 and GFAP), muscle cells (expressing SMA), cartilage (expressing collagen type II), exocrine glandular cells (expressing amylase and trypsin), endocrine glandular cells (expressing insulin), and epidermal cells (expressing cytokeratin), following organoid body formation,

does not reasonably provide enablement for

isolated pluripotent adult stem cells from any species of vertebrate obtained from any exocrine gland tissue, wherein said pluripotent adult stem cells differentiate into any cell type.

The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Enablement is considered in view of the Wands factors (MPEP 2164.01(a)). The court in Wands states: "Enablement is not precluded by the necessity for some experimentation such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue,' not 'experimentation.' " (*Wands*, 8 USPQ2d 1404). Clearly, enablement of a claimed invention cannot be predicated on the basis of quantity of experimentation required to make or use the invention. "Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations." (*Wands*, 8 USPQ2d 1404). The factors to be considered in determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount or direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. While all of these factors are considered, a sufficient amount for a *prima facie* case are discussed below.

The claims broadly encompass pluripotent adult stem cells from any species of vertebrate. However, at the time of filing, the art teaches that an artisan cannot reasonably predict that stem cells obtained from different species of animals necessarily have the same characteristics. For example, Pera et al., 2000, Journal of Cell Science,

113: 5-10, teach generic criteria for pluripotent ES or EG cells (Pera et al., page 6, box) and teach that only mouse EG or ES cells meet the four criteria, while primate ES cells meet the first three of four criteria (Pera et al., pages 6-7, under "A generic functional definition of an ES cell"). As such, Pera et al. teach that while ES cells from mice and humans have been obtained, the ES cells from two different species of vertebrates do not necessarily behave the same way. As such, while the specification teaches that pluripotent cells obtained from rat and human pancreas differentiated into cells that expressed PGP 9.5, NF, S100, GFAP, SMA, collagen type II, amylase, trypsin, insulin, and cytokeratin following organoid body formation (specification, page 17, 2nd parag.), the specification does not teach that cells from other species of animals would necessarily differentiate into the same cell types. Thus, the specification does not provide guidance to practice the full breadth of the claimed invention.

The claims are broadly drawn to cells obtained from any exocrine glandular tissue. However, at the time of filing, the art teaches that adult stem cells obtained from a variety of tissues do not have the same differentiation potential (Henningson, et al., 2003, Journal of Allergy and Clinical Immunology, 111, supplement 2: 745, 753, Table 1, point 3). For example, Jiang et al., 2002, Nature, 418: 41-49, see IDS, teach that pluripotent cells from adult marrow differentiate into endothelium, neuroectoderm, and hepatocytes (Jiang et al., pages 42-43, under "In vitro differentiation of single mMAPCs and rMAPCs"), while Zuk et al., 2002, Molecular Biology of the Cell, 13: 4279-4295, teach that pluripotent cells obtained from adipose tissue differentiated into adipocytes, osteocytes, chondrocytes, myocytes, and neuronal cells (Zuk et al., table 1). As this

issue applies to the instant invention, the art teaches that pluripotent cells from different tissue sources have different differentiation ability that an artisan cannot reasonably predict that pluripotent cells, obtained from other exocrine glandular tissue would necessarily behave the same way. As such, the specification does not provide guidance for an artisan to practice the full breadth of the claimed invention.

Thus, for these reasons, the claims are rejected.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-14 are rejected under 35 U.S.C. 102(b) as being anticipated by Schneider et al., 2001, Am. J. Physiol. Cell. Physiol., 281: C532-C543, see IDS, as evidenced by Kruse et al., 2004, Appl. Phys. A, 79: 1617-1624, see IDS.

Schneider et al. teach that pancreatic stellate cells were isolated by density gradient centrifugation after collagenase digestion of rat pancreas or by the outgrowth method using pancreas tissue of rats with cerulein pancreatitis (Schneider et al., page C533, 2nd col., 1st parag. under "Cell Isolation and Culture").

Kruse et al. teach that the pluripotent pancreatic cells described in their publication correspond to the pancreatic stellate cells (PSCs) previously described in

references 4, 5, 7, 8. Note that Schneider et al. is reference 7 (Kruse et al., page 1621, 3rd col., 1st parag. under "Isolation, proliferation and self-renewal of PSLCs and OBs"). It is noted that the Kruse et al. publication teach the same steps used to isolate pancreatic stem cells as that described in the specification (Kruse et al., pages 1617-1618, under "Cell Isolation" and specification, Example 2). Because Kruse et al. teach that the cells taught in the publication (and thus, the specification) are the same as those isolated by Schneider et al., Schneider et al. anticipate the claimed invention.

While Schneider et al. do not specifically disclose specific characteristics such as those listed in the claims, e.g. that the PSCs can form organoid bodies, differentiate into three germ layers, and exhibit unlimited division, it is presumed that the cells taught by Schneider et al. have these characteristics because they are the same as those taught in the specification. Where, as here, the claimed and prior art products are identical or substantially identical, or are produced by identical or substantially identical processes, the PTO can require an applicant to prove that the prior art products do not necessarily or inherently possess the characteristics of his claimed product. See In re Ludtke 441 F.2d 660, 169 USPQ 563 (CCPA 1971). Whether the rejection is based on "inherency" under 35 USC 102, or "prima facie obviousness" under 35 USC 103, jointly or alternatively, the burden of proof is the same, and its fairness is evidenced by the PTO's inability to manufacture products or to obtain and compare prior art products. In re Best, Bolton, and Shaw, 195 USPQ 430, 433 (CCPA 1977) citing In re Brown, 59 CCPA 1036, 459 F.2d 531, 173 USPQ 685 (1972).

Claims 1-14 rejected under 35 U.S.C. 102(b) as being anticipated by Apte et al., 1998, Gut, 43: 128-133, see IDS, as evidenced by Kruse et al., 2004, Appl. Phys. A, 79: 1617-1624, see IDS.

Apte et al. teach that pancreatic stellate shaped cells were isolated from pancreatic tissue from rats. The tissue was minced, digested with enzymes, passed through narrow orifices, and filtered through nylon mesh. The cells were then spun in a centrifuge and plated (Apte et al., page 129, 2nd col., parag. under "Isolation and Culture of Pancreatic Stellate Shaped Cells").

Kruse et al. teach that the pluripotent pancreatic cells described in their publication correspond to the pancreatic stellate cells (PSCs) previously described in references 4, 5, 7, 8. Note that Apte et al. is reference 8 (Kruse et al., page 1621, 3rd col., 1st parag. under "Isolation, proliferation and self-renewal of PSLCs and OBs"). It is noted that the Kruse et al. publication teach the same steps used to isolate pancreatic stem cells as that described in the specification (Kruse et al., pages 1617-1618, under "Cell Isolation" and specification, Example 2). Because Kruse et al. teach that the cells taught in the publication (and thus, the specification) are the same as those isolated by Apte et al., Apte et al. anticipate the claimed invention.

While Apte et al. do not specifically disclose specific characteristics such as those listed in the claims, e.g. that the PSCs can form organoid bodies or differentiate into three germ layers, and exhibit unlimited division, it is presumed that the cells taught by Apte et al. have these characteristics because they are the same as those taught in the specification. Where, as here, the claimed and prior art products are identical or

substantially identical, or are produced by identical or substantially identical processes, the PTO can require an applicant to prove that the prior art products do not necessarily or inherently possess the characteristics of his claimed product. See In re Ludtke 441 F.2d 660, 169 USPQ 563 (CCPA 1971). Whether the rejection is based on "inherency" under 35 USC 102, or "prima facie obviousness" under 35 USC 103, jointly or alternatively, the burden of proof is the same, and its fairness is evidenced by the PTO's inability to manufacture products or to obtain and compare prior art products. In re Best, Bolton, and Shaw, 195 USPQ 430, 433 (CCPA 1977) citing In re Brown, 59 CCPA 1036, 459 F.2d 531, 173 USPQ 685 (1972).

Claims 1-8, 13, 14 are rejected under 35 U.S.C. 102(b) as being anticipated by Bachem et al., 1998, Gastroenterol., 115: 421-432, see IDS, as evidenced by Kruse et al., 2004, Appl. Phys. A, 79: 1617-1624, see IDS.

Bachem et al. teach that human PSCs were isolated by outgrowth using explant techniques from histologically fibrotic areas of the pancreas. Small tissue blocks were cut from the pancreas and after reculturing, PCSs grew out from the tissue blocks, 1-3 days later (Bachem et al., page 422, 1st parag. under "Cell Isolation").

Kruse et al. teach that the pluripotent pancreatic cells described in their publication correspond to the pancreatic stellate cells (PSCs) previously described in references 4, 5, 7, 8. Note that Bachem et al. is reference 4 (Kruse et al., page 1621, 3rd col., 1st parag. under "Isolation, proliferation and self-renewal of PSLCs and OBs"). It is noted that the Kruse et al. publication teach the same steps used to isolate

pancreatic stem cells as that described in the specification (specification, Example 2). Because Kruse et al. teach that the cells taught in the publication (and thus, the specification) are the same as those isolated by Bachem et al., Bachem et al. anticipate the claimed invention.

While Bachem et al. do not specifically disclose specific characteristics such as those listed in the claims, e.g. that the PSCs can form organoid bodies or differentiate into three germ layers (e.g. claims 7 and 8), it is presumed that the cells taught by Bachem et al. have these characteristics because they are the same as those taught in the specification. Where, as here, the claimed and prior art products are identical or substantially identical, or are produced by identical or substantially identical processes, the PTO can require an applicant to prove that the prior art products do not necessarily or inherently possess the characteristics of his claimed product. See In re Ludtke 441 F.2d 660, 169 USPQ 563 (CCPA 1971). Whether the rejection is based on "inherency" under 35 USC 102, or "prima facie obviousness" under 35 USC 103, jointly or alternatively, the burden of proof is the same, and its fairness is evidenced by the PTO's inability to manufacture products or to obtain and compare prior art products. In re Best, Bolton, and Shaw, 195 USPQ 430, 433 (CCPA 1977) citing In re Brown, 59 CCPA 1036, 459 F.2d 531, 173 USPQ 685 (1972).

However, with regard to the claims being drawn to cells that exhibit "unlimited division" after cryopreservation (claim 9) or stable proliferation (claim 10), Kraus et al. specifically teach that Bachem et al. do not teach the claimed invention. Kraus et al. indicate that cells obtained from tissue blocks do not proliferate as well cells from

isolated exocrine acini and could not be stored after 3-20 passages at temperatures below –130°C without losing their viability and capacity for differentiation (Kraus et al., page 1621, 3rd col., 1st parag. under "Isolation, proliferation and self-renewal of PSLCs and OBs") and thus, Bachem et al. do not anticipate claims to unlimited division or stable proliferation of the cells (e.g. claims 9 and 10). Claims 11 and 12 depend on claim 10.

Conclusion

No claims allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joanne Hama, Ph.D. whose telephone number is 571-272-2911. The examiner can normally be reached Monday through Thursday and alternate Fridays from 9:00-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Peter Paras, can be reached on 571-272-4517. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight

(EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public. For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

JH

ANNE M. WEHBE' PH.D
PRIMARY EXAMINER